Citation:

Cho E, Chen WY, Hunter DJ, Stampfer MJ, Colditz GA, Hankinson SE, Willett WC. Red meat intake and risk of breast cancer among premenopausal women. Arch Intern Med. 2006 Nov 13;166(20):2253-9.

PubMed ID: 17101944

Study Design:

Prospective cohort study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To assess red meat intake and breast cancer risk among premenopausal women.

Inclusion Criteria:

Female registered nurses participating in The Nurses' Health Study II

- 25 to 42 years of age
- living in 1 of 14 states in the United States when they responded in 1989 to a questionnaire regarding their medical histories and lifestyles.

Exclusion Criteria:

Exclusion criteria

- Women who had an implausible total energy intake (<800 or >4200 kcal/d)
- Women who left more than 70 food items blank on the 1991 food frequency questionnaire
- Women who reported a diagnosis of cancer, except nonmelanoma skin cancer, before returning the 1991 questionnaire
- Postmenopausal women at baseline
- Women after they reached either natural or surgical (bilateral oophorectomy with or without hysterectomy) menopause during follow-up.
- Women who had undergone a hysterectomy but not a bilateral oophorectomy were also excluded at the time of surgery because their menopausal status was unknown.

Description of Study Protocol:

Recruitment Subjects were participants of The Nurses Health Study II

Design Prospective Cohort Study

Statistical Analysis

- Participants contributed person-time from the date of return of the 1991 questionnaire until the date of breast cancer diagnosis, death, menopause (natural or surgical), or June 1, 2003, whichever came first.
- Participants were divided into categories according to their red meat intake.
- Relative risks (RRs) of breast cancer were calculated as the incidence rate for a given category of red meat intake compared with the rate among participants in the lowest category of intake.
- Cox proportional hazards regression were used to account for potential effects of other risk factors for breast cancer.
- To control as finely as possible for confounding by age, calendar time, and any possible 2-way interactions between these 2 time scales, analysis were stratified jointly by age in months at the start of each follow-up period and calendar year of the current questionnaire cycle.
- Multivariate models also simultaneously adjusted for tobacco use, body mass index (calculated as weight in kilograms divided by the square of height in meters), height, age at menarche, oral contraceptive use, family history of breast cancer, history of benign breast disease, parity and age at first birth, and intakes of calories and alcohol.
- The SAS PROC PHREG program was used for all analyses, and the Anderson-Gill data structure was used to handle time-varying covariates efficiently, with a new data record created for every questionnaire cycle at which a participant was at risk and covariates set to their values at the time the questionnaire was returned.
- For all RRs, 95% confidence intervals (CIs) were calculated.
- Tests for trend were conducted using the median value for each category of food or food group as a continuous variable.
- A test of the difference in the estimates of red meat intake (median values for each category as a continuous variable) for hormone receptor status was conducted by using the squared *t* statistic, which has a ^{2} distribution with 1 *df*.
- All *P* values were 2 sided.

Data Collection Summary:

Timing of Measurements

- A semiquantitative FFQ with more than 130 food items was sent to women in 1991, 1995, and 1999 to assess usual dietary intake during the past year.
- 1991 intake was used for the 1991 to 1995 follow-up periods, the average of 1991 and 1995 intake was used for the 1995 to 1999 follow-up periods, and the average of all 3 was used for the 1999 to 2003 follow-up periods to maintain a strictly prospective analysis.

Dependent Variables

- Variable 1: Breast cancer was identified by biennial questionnaires mailed between 1993 and 2003.

- Once reported permission to access pathologic reports was obtained.

Independent Variables Intakes of total red meat and individual red meat items, including beef or lamb as a main dish; pork as a main dish; beef, pork, or lamb as a sandwich or mixed dish; hamburger; bacon; hot dogs; and other processed meats were obtained with the FFQ.

Description of Actual Data Sample:

Initial N: 116671 females

Attrition (final N):A total of 90 659 premenopausal women were included in the analysis at baseline.

Age: 36.0± 4.6 (Mean ± SD) 26 to 46 years (range)

Summary of Results:

- The highest intake of red meat was weakly and non-significatly associated with elevated risk of everall breast cancer. (*P*=0.01)
- However, when cases were divided according to Estrogen Receptor and Progesterone Receptor status higher red meat intake was strongly related to an increased risk of ER+/PR+ breast cancers but not ER–/PR– cancers.
- Almost all of the individual red meat items had statistically significant positive trends of increasing ER+/PR+ breast cancer risk.

Author Conclusion:

In this population of relatively young, premenopausal women, red meat intake was associated with a higher risk of hormone receptor–positive breast cancer but not with risk of hormone receptor–negative cancer.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes

2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	N/A
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	N/A
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes

3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	N/A
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	N/A
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	N/A
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	N/A
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	N/A
9.1.	Is there a discussion of findings?	Yes

	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes